Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS

1. to 31. (Canceled)

- (currently amended): A pair of oligonucleotide probes (K) comprising:
 - a first oligonucleotide probe (P1) that comprises
 - a first clamp segment (C1), that is capable of hybridizing to a second clamp segment (C2) of a second oligonucleotide probe (P2), and
 - (ii) a first target segment (T1) at its 3° end that is capable of hybridizing to a first segment (S1) of a target DNA sequence (D) to be detected;
 - (b) a second oligonucleotide probe (P2) that comprises
 - (i) a second clamp segment (C2), that is capable of hybridizing to C1, and
 - a second target segment (T2) at it's 5' end that is capable of hybridizing to a second segment (S2) of D

wherein S1 and S2 are located essentially adjacent to one another in D, and wherein the <u>5' end of S1 is adjacent to 3' end of the T1 and the 5' end of T2 are capable of being ligated to each other when the 3' end of <u>S2T1 and the 5' end of T2 are hybridized to S1 and S2</u>, respectively.</u>

33. to 34. Canceled

- 35. (previously presented): A pair of oligonucleotide probes according to claim 32, wherein C1 and C2 when hybridized to each other have a melting temperature T_{mc} which is higher than the melting temperature T_{mt} of each of T1 and T2 when hybridized to a complementary DNA sequence.
- 36. (previously presented): A pair of oligonucleotide probes according to claim 35, wherein the T_{mc} of hybridized C1 and C2 is at least 1°C higher than the highest T_{mt} of hybridized T1 and T2.
- 37. (previously presented): The pair of nucleotide probes of claim 36 wherein the T_{mc} of hybridized C1 and C2 is at least 5°C higher than the highest T_{mt} of hybridized T1 and T2.

Appln. No. 10/560,968 Response dated June 14, 2010 Reply to Office Action of Feb. 19, 2010

- 38. (previously presented): The pair of nucleotide probes of claim 37 wherein the T_{mc} of hybridized C1 and C2 is at least 10°C higher than the highest T_{mt} of T1 and T2.
- 39. (previously presented): A pair of oligonucleotide probes according to claim 32 wherein the guanylic acid and cytidylic acid (GC) content of C1 and C2 ranges from more than 50% to 100%.
- (previously presented): A pair of oligonucleotide probes according to claim 39 wherein the GC content of C1 and C2 is >60%.
- 41. (previously presented): A pair of oligonucleotide probes according to claim 40 wherein the GC content of C1 and C2 is >70%.
- 42. (previously presented): A pair of oligonucleotide probes according to claim 40 wherein the GC content of C1 and C2 is >80%.
- 43. (previously presented): A pair of oligonucleotide probes according to claim 40 wherein the GC content of C1 and C2 is between 90% and 100%.
- 44. (previously presented): A pair of oligonucleotide probes according to claim 32, wherein C1 and C2 comprise, at least one G or C nucleotide more than the number of G or C nucleotides in T1 or T2 of the same length.
- 45. (previously presented): A pair of oligonucleotide probes according to claim 44 wherein C1 and C2 comprise at least two G or C nucleotides more than the number of G or C nucleotides in T1 or T2 of the same length.
- 46. (previously presented): A pair of oligonucleotide probes according to claim 45 wherein C1 and C2 comprise at least three G or C nucleotides more than the number of T1 or T2 of the same length.
- 47. (previously presented): A pair of oligonucleotide probes according to claim 46 wherein C1 and C2 comprise at least four G or C nucleotides more than the number of T1 or T2 of the same length.
- 48. (previously presented): A pair of oligonucleotide probes according to claim 47 wherein C1 and C2 comprise at least five G or C nucleotides more than the number of T1 or T2 of the same length.

Appln. No. 10/560,968 Response dated June 14, 2010 Reply to Office Action of Feb. 19, 2010

- 49. (previously presented: A pair of oligonucleotide probes according to claim 32, wherein the C1 and/or C2 comprises modified nucleotides that have an increased binding affinity compared to conventional adenylic acid (A), thymidilic acid (T), cytidylic acid (C) and guanylic acid (G).
- 50. (previously presented): A pair of oligonucleotide probes according to claim 32, wherein the length of C1 and/or C2 is from 10 to 30 nucleotides.
- 51. (previously presented): A pair of oligonucleotide probes according to claim 50, wherein the length of T1 and T2 is, independently, 15 to 30 nucleotides.
- (previously presented): A pair of oligonucleotide probes according to claim 32, wherein
 P1, P2 or both includes at least one primer binding site designated B1 or B2, respectively.
- 53. (previously presented): A pair of oligonucleotide probes according to claim 32, wherein P1 and P2 include at least one stuffer sequence designated R1 or R2, respectively.
- 54. (previously presented): A pair of oligonucleotide probes according to claim 32, wherein the each of T1 and T2 includes at least one allele-specific nucleotide.
- 55. (previously presented): A pair of oligonucleotide probes according to claim 54, wherein the allele-specific nucleotide is located at the end of T1 or of T2.
- 56. (previously presented): A set of oligonucleotide probes comprising the pair of oligonucleotides according to claim 54 and at least one additional probe (P3) that includes a target segment T3 having an additional allele specific nucleotide and wherein P3 is distinct from P1 and P2.
- 57. (previously presented): A pair of oligonucleotides probes according to claim 32, wherein P1 or P2 comprises an additional region that cannot anneal to D, which additional region is located at the end of P1 or P2 at a position that corresponds to a junction site between S1 and S2.
- 58. (previously presented): A pair of oligonucleotides probes according to claim 57, wherein the additional region creates a cleavable site which site will be cleaved when exposed to a cleaving agent under conditions wherein cleavage can occur.

Appln. No. 10/560,968 Atty Dkt: VAN EIJK-17

Response dated June 14, 2010 Reply to Office Action of Feb. 19, 2010

59. (previously presented): A group of oligonucleotides comprising at least two pairs of probes according to claim 32, wherein the clamp segments C1 and C2 of each pair of probes are designed such that for each probe pair, the combination of C1 and C2 forms a unique combination within the group such that each probe can selectively hybridize to one other probe in the group.

- 60. (previously presented): A group of oligonucleotides according to claim 59, wherein each C1 and C2 of each pair of probes further includes a unique sequence.
- 61. (previously presented): A method for the detection of a target nucleotide sequence (D) in a sample comprising the steps of:
 - (a) adding to the sample a pair (K) of probes according to claim 32;
 - (b) allowing the probes to hybridize to the target sequence;
 - (c) ligating T1 and T2 when they are located adjacent to one another when annealed to D
 to form ligation products; and
 - (d) detecting the presence or absence of any ligation products.
- (previously presented): A method according to claim 61, wherein the ligation products are amplified prior to the detecting step (d).
- 63. (previously presented): A method according to claim 61, wherein D is amplified prior to hybridization of the probes.
- 64. (previously presented): A method according to claim 61, wherein the sample includes more than one target nucleotide sequence designated D1...Dn, respectively, and wherein a group of more than one pair of oligonucleotide probes designated K1...Kn, respectively that correspond to, and are capable of binding to and detecting, D1...Dn, respectively, are added to the sample in step (a).
- 65. (previously presented): A method according to claim 64 wherein the clamp segments C1 and C2 of each pair of probes K1...Kn are designed such that for each probe pair K1...Kn, the combination of C1 and C2 forms a unique combination within the group such that for each probe pair K1...Kn, the probe P1 can selectively hybridize to a unique single probe P2 in the group and not to any other probe P2 in the group.
- 66. (previously presented): A method according to claim 61 wherein each probe includes a unique sequence.

- 67. (previously presented): A method according to claim 61 wherein detection is based on measurement or assessment of nucleic acid length, sequence and/or mass.
- 68. (previously presented): A method according to claim 61 wherein the target sequence D is in a DNA or RNA molecule.
- 69. (previously presented): A method according to claim 68 wherein the DNA or RNA molecule is in the form of polyA+RNA, cDNA, genomic DNA, organelle DNA, a synthetic nucleic acid, a DNA library, a clone bank or any combination thereof.
- 70. (previously presented): A set of at least three oligonucleotides suitable for SNP genotyping, comprising:
 - (a) a first oligonucleotide probe (P1) that comprises
 - a first clamp segment (C1) that is capable of hybridizing to a second clamp segment (C2) of a second oligonucleotide probe (P2), and
 - (ii) a first target segment (T1) that is capable of hybridizing to a first segment
 (S1) of a target DNA sequence (D) to be detected;
 - (b) a second oligonucleotide probe (P2) that comprises
 - (i) a second clamp segment (C2) that is capable of hybridizing to C1, and
 - a second target segment (T2) that is capable of hybridizing to a second segment (S2) of D;
 - (c) at least a third oligonucleotide probe (P3) that comprises C2 and T2;
 wherein P2 and P3 include an allele-specific nucleotide, located at the end of T1 or T2; and

wherein the allele-specific nucleotide of P2 and P3 corresponds to the alleles of the SNP to be detected; and

wherein P2 and P3 further include a stuffer segment that discriminates between amplified ligation products formed between P1 and P2 or P1 and P3.

- 71. (previously presented): A kit useful in a method for detecting the presence, absence or amount of a target DNA sequence in a sample, the kit comprising at least one pair of probes as defined in claim 32 and one or more reagents to be used in said detecting method.
- 72. (previously presented): A kit useful in a method for detecting the presence, absence or amount of a target DNA sequence in a sample, the kit comprising at least one group of probes as defined in claim 59 and one or more reagents to be used in said detecting method.